

REMARKS

Claims 45-53 are amended herein to correct informalities in the claims. New claims 54-61, directed to a method of treatment using the claimed compounds are added herein in response to the Examiner's statement that method claims may be added in response to the Office Action, which will be joined with the compound claims if allowed. New claims 54-61 are supported by original claims 34-37, 39 and 41. Hence no issues of new matter are presented. Accordingly, Applicants respectfully request joinder thereof.

I. Priority

The Examiner did not acknowledge Applicants' claim for foreign priority or receipt of the certified copies of the priority documents. Applicants respectfully request formal acknowledgement of the same in the next Office Action.

II. Claim Rejections Under 35 U.S.C. § 103

On page 3 of the Office Action, claims 45-53 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Napoli et al (HCAPLUS Document No. 105:187053). The Examiner asserts that the disclosed vitamin D3 compounds embrace Applicants' claimed compounds. The Examiner asserts that the disclosed compounds have a side chain that is similar to that instantly claimed. The Examiner further asserts that the claimed compounds are a specific species or subgenus of the claimed compounds.

It is the Examiner's position that it would have been obvious to one of ordinary skill in the art to select any of the species of the genus taught by the reference with a reasonable expectation that the species would have properties similar to that of the genus.

Applicants' respectfully traverse the rejection. Applicants submit that the Examiner has not made a *prima facie* showing of obviousness on the record. To make a *prima facie* case of obviousness, the Examiner must satisfy three criteria. First, the cited references must teach or suggest the motivation to modify the primary reference or combine the references to make the claimed invention. Second, there must be a reasonable expectation of success to do so. Finally, the combination of the references must teach or suggest all of the claim limitations.

In this case, there is no motivation or suggestion in the cited reference to modify the disclosed compound to achieve the claimed invention. The fact that references can be modified is not sufficient to establish *prima facie* obviousness. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). It is also insufficient to establish *prima facie* obviousness based on the assertion that a modification is within the capabilities of one of ordinary skill in the art without an objective reason to make the modification. See *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993); *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000); *Al-Site Corp. v. VSI int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999); and MPEP § 2143.01.

Further, the mere fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. A proper analysis requires a determination of whether there is motivation to select the specifically claimed compound from the disclosed genus.

In view thereof, Applicants submit that the functional moiety R₅₁ at the 25 position of the claimed compounds differs from that of the cited reference. As described in the specification on page 5 line 28 to page 6, line 7, the claimed vitamin D₃ derivative compounds have a suppressing

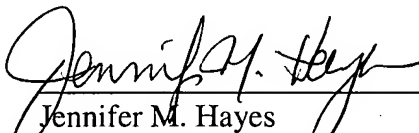
Amendment Under 37 C.F.R. § 1.111
U.S. Application No. 10/035,211

effect on neutrophilic infiltration and are effective as treating agents for inflammatory respiratory diseases. The reference does not teach the disclosed compounds have a suppressing effect on neutrophilic infiltration and therefore provides no motivation for modifying the disclosed compounds with a reasonable expectation of success in achieving the claimed vitamin D₃ compounds, having the unexpected suppressing effect on neutrophilic infiltration. Therefore, there is no motivation for one of ordinary skill in the art to specifically select the presently claimed compounds based upon the disclosure of Napoli. The Examiner's conclusion of obviousness is therefore based upon improper hindsight reasoning.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,


Jennifer M. Hayes
Registration No. 40,641

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE



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PATENT TRADEMARK OFFICE

Date: January 10, 2003

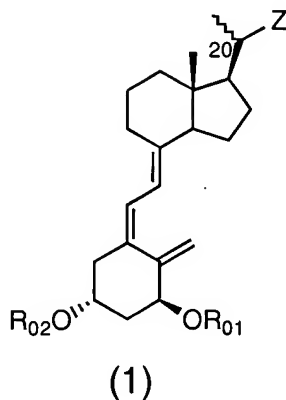
APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

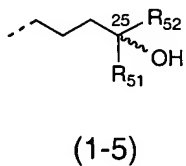
The claims are amended as follows:

45. (Amended) A vitamin D₃ ~~derivatives~~ compound expressed by the following general formula ~~{1}~~(1) or pharmaceutically permissible solvates thereof,



—wherein, R₀₁ and R₀₂ are each independently a hydrogen atom, a trimethylsilyl group, a triethylsilyl group, a t-butyldimethylsilyl group, an acetyl group, a methoxymethyl group or a tetrahydro-4H-pyran-2-yl group;

Z is represented by formula (1-5),



{in the above formula (1-5),

R_{51} expresses $-\text{CONR}_{511}\text{R}_{512}$, $-\text{COR}_{513}$ or $-\text{C}(\text{OH})\text{R}_{514}\text{R}_{515}$, wherein R_{511} and R_{512} are identical to or different from each other, and they are a hydrogen atom or a C_1 - C_4 alkyl group, or both the members together express a nitrogen-containing C_3 - C_8 alkyl ring or a morpholino group in cooperation with the nitrogen atom to which they are bonded; and R_{513} , R_{514} and R_{515} are identical to or different from each other, and they express a C_1 - C_4 alkyl group;

R_{52} expresses a methyl group, an ethyl group, a trifluoromethyl group or a pentafluoroethyl group.}}

46. (Amended) A vitamin D_3 ~~derivative~~ compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R_{01} and R_{02} are both hydrogen atoms.

47. (Amended) A vitamin D_3 ~~derivative~~ compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R_{51} is $-\text{CONR}_{511}\text{R}_{512}$ or $-\text{COR}_{513}$.

48. (Amended) A vitamin D_3 ~~derivative~~ compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R_{51} is $-\text{CONR}_{511}\text{R}_{512}$.

49. (Amended) A vitamin D_3 ~~derivative~~ compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R_{51} is $-\text{COR}_{513}$.

50. (Amended) A vitamin D_3 ~~derivative~~ compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R_{51} is $-\text{CONR}_{511}\text{R}_{512}$, and R_{511} and R_{512} are identical to or different from each other, and they are a

Amendment Under 37 C.F.R. § 1.111
U.S. Application No. 10/035,211

methyl group or an ethyl group, or both the members together express an aziridine, pyrrolidine, ~~piperietine~~-piperidine or morpholino ring in cooperation with the nitrogen atom to which they are bonded.

51. (Amended) A vitamin D₃ ~~derivative~~-compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R₅₁ is COR₅₁₃, and R₅₁₃ is a methyl group or an ethyl group.

52. (Amended) A vitamin D₃ ~~derivative~~-compound or a pharmaceutically permissible solvate thereof described in Claim 45, wherein, in the above formula (1), R₅₂ is a methyl group.

53. (Amended) A pharmaceutical composition ~~composed of~~comprising a vitamin D₃ ~~derivative~~-compound or pharmaceutically permissible solvate thereof described in Claim 45, and a pharmaceutically permissible carrier.

Claims 54-61 are added as new claims.

APPENDIX

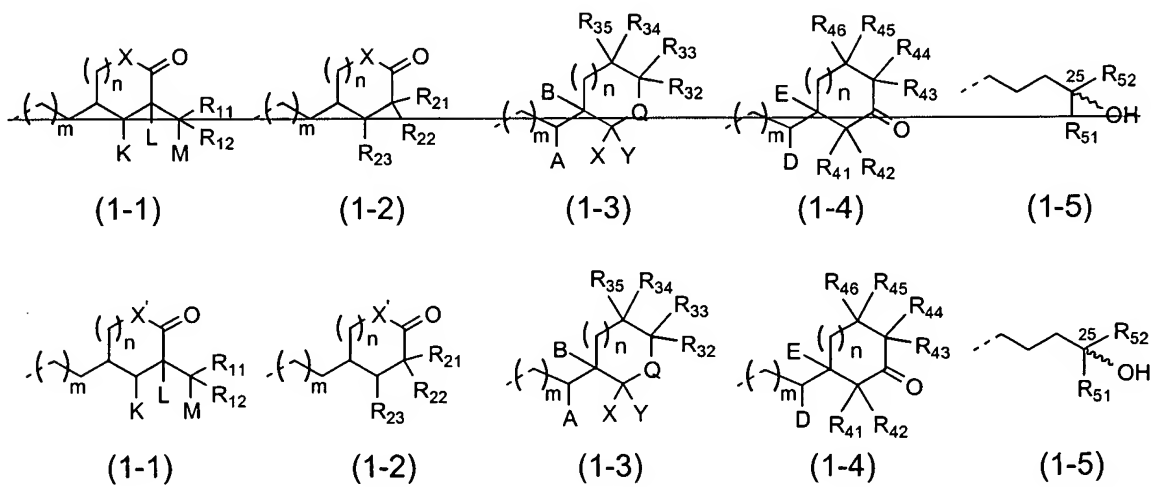
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

This is a Divisional of Application No. 09/830,167 filed April 23, 2001, the disclosure of which is incorporated herein by reference.

Page 6, the paragraph at lines 18-19 with formulas (1-1) to (1-5), and replace it with the following new paragraph:



IN THE CLAIMS:

Please cancel claims 1-44

New claims 45-53 are added.

IN THE ABSTRACT OF DISCLOSURE:

The abstract is changed as follows: